REMARKS

The status of the application is as follows: claims 1-9 and 25-30 are pending. Claims 10-24 were withdrawn from consideration pursuant to an earlier election. Claims 1, 5, 6, 8, 9, 25 and 27 were amended and new claim 30 was added in the response filed February 3, 2006. Claims 24 and 25 are amended to correct minor typographical errors and new claims 31-37 are added in this Supplemental Amendment. Entry and consideration of the amendments and new claims are earnestly requested.

Applicant takes this opportunity to thank the Examiner for the courtesies extended in the telephone interview of May 23, 2006. During the interview, Dr. Minden explained the claimed biomolecule capture device and the differences between it and the references cited in the Office Action of October 4, 2005. The capture device is particularly useful in the field of proteomics and can be used, for example, to isolate an entire set of proteins in a solution and to allow the option of separation of unmodified proteins from the solution. The conventional methods use precipitation to separate proteins from a multi-component solution. Such methods are not satisfactory because not all proteins will precipitate and not all precipitated proteins will go back into solution. *See*, the Specification of the Subject application at the paragraph bridging pages 3-4. The differences between the biomolecule capture device of the Subject Application and the references cited in the October 2005 Office Action are summarized below.

The Examiner had rejected (i) claims 1-4 and 7-9 under 35 U.S.C. §102(b) as being anticipated by Singh et al., 203 Arch. Biochem. Biophys. 774 (1980), (ii) claims 1-3, 5-9, 25 and 27-29 under 35 U.S.C. §102(e) as being anticipated by Johnson et al., U.S. Patent No. 6,372,813, and (iii) claims 5-6 and 25-29 under 35 U.S.C. §103(a) as being unpatentable over Singh et al. in view of Kinsella & Shetty, U.S. Patent No. 4,348,479.

The Singh et al. article differs from the claimed biomolecule capture device because Singh et al. use a maleimido group attached to an agarose support via a cleavable phenyl ester linkage and binds thiol groups of proteins covalently through the ethylene portion of the maleimido group. When the proteins are separated from the agarose, the phenyl ester linkage is cleaved and a maleimido protein derivative is released, which would then require further processing to yield the unmodified protein. *See* the Singh et al. Abstract. Contrary to the

Examiner's characterization of the Singh et al. article, the maleimido group used by Singh et al. is different from the maleic anhydride compound of the claimed biomolecule capture device. Referring to Figures 1 and 2 of the Subject Application, a maleic anhydride has an oxygen molecule in the position held by a nitrogen molecule in the maleimido group shown on page 775 of the Singh et al. article. The Examiner will also note, by comparing those structures, that the maleimide of the Singh et al. MPE-Agarose orients the double bond (*i.e.*, the ethylene portion of the molecule) in a position for reaction with the thiol groups of proteins and the nitrogen side is oriented toward the substrate. Only about 90% of proteins, for example, contain thiols, so the Singh et al. device can not bind all proteins. In the claimed capture device of the Subject Application, the anhydride portion of the maleic anhydride is oriented for binding to biomolecules. Referring to Figure 2, binding occurs via the primary amines of biomolecules. All proteins, for example, contain primary amines, so the capture device of the Subject Application can capture all proteins and other biomolecules containing amines. *See*, the Specification at page 7, lines 8-10 for the definition of "biomolecules." When the biomolecules are to be released, the bond between the biomolecule and the maleic anhydride (and not the bond between the support and the maleic anhydride compound) can be reversed to free unmodified biomolecules[1].

The structure and therefore the chemistry involved in the bond between the maleimido group and the agarose and between the maleimido group and the proteins to which it may bind are thus very different from the structure and the chemistry that results from the covalent bond between the support and the maleic anhydride compound and between the maleic anhydride compound and the biomolecules which may bind thereto in the capture device claimed in the Subject Application. Applicant submits that the claimed biomolecule capture device is not anticipated by the Singh et al reference. Withdrawal of the rejection of claims 1-4 and 7-9 under 35 U.S.C §102(b) is requested.

The Johnson patent also employs a maleimide compound attached to a support in the same orientation as that used in the Singh et al. article. Referring to Figs. 3 and 4 and col. 8, lines 22-25, the Johnson patent uses photoaddition to create a permanent carbon-carbon bond

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[1] With the exception of the intentional modification of biomolecules described at page 13 of the Specification. Such modification is not required for separation of the biomolecules.

between the maleimide attached to the support and the biomolecule, such as DNA. Unlike the reversible covalent bonds between biomolecules and the maleic anhydride compound of the claimed capture device, the carbon-carbon bonds of the Johnson patent are irreversible. Applicant submits that the claimed biomolecule capture device is not anticipated by the Johnson patent. Withdrawal of the rejection of claims 1-3, 5-9, 25 and 27-29 under 35 U.S.C §102(e) is requested.

The Kinsella et al. patent, which is discussed in the Background section of the Subject Application, describes the use of a maleic anhydride to bind protein, but the maleic anhydride is not attached to a support. It is added drop wise to a solution of protein-nucleic acid mixture. Although the reaction takes place through the anhydride portion of the compound, Kinsella takes primary amines and converts them to carboxylic acid to change the ionic characteristics of the protein so that the proteins will precipitate. The resulting protein from Kinsella's use of maleic anhydride is a derivatized, or modified, protein. Further processing by precipitation is required. Thus, Kinsella et al. present the same types of problems that applicant sought to overcome with the capture device of the Subject Application.

The combination of the teachings of Singh et al. with the teaching of Kinsella et al., as proposed by the Examiner, would not result in the claimed capture device. There is no teaching to re-orient the maleic anhydride if it were substituted for the maleimido group used by Singh et al. so that the double bond portion is oriented toward the substrate rather than being available for reaction with biomolecules. There is nothing in either reference that teaches or suggests that the maleimido group, or the maleic anhydride if it were to be attached to the agarose support of Singh et al., should not form a cleavable bond with the support. There is no teaching or suggestion to avoid a change in the ionic characteristics of the proteins to prepare them for precipitation. Neither the Singh et al. article nor Kinsella et al. patent taught or suggested a structure for a capture device that would avoid the need for precipitation to isolate unmodified proteins. Finally, applicant notes that both the Singh et al. article and the Kinsella et al. patent were submitted and filed, respectively, in 1980. While both sought a way to separate proteins from a multi-component solution, neither achieved that goal for all proteins and neither achieved the goal of a relatively easy and rapid separation and isolation of unmodified proteins. During the 20 plus years since their work, those skilled in the art have not, to applicant's knowledge,

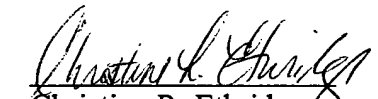
until applicant's invention, advanced past the conventional precipitation methods for separation and isolation of proteins. Applicant submits that the long felt, but unmet need in the art for a better, more rapid means of separating and isolating biomolecules is evidence of the nonobviousness of the biomolecule capture device claimed in the Subject Application. For the foregoing reasons, applicant submits that the claimed biomolecule capture device is not obvious in view of the teachings of the Singh et al. and Kinsella et al. references. Withdrawal of the rejection of claims 5-6 and 25-29 under 35 U.S.C §103(a) is requested.

New claims 31-37, submitted herewith, find support in the original claims, the title (...Reversible Capture of Biomolecules), in the structures shown in Figures 1 and 2 of the Subject Application, and throughout the Specification, such as, page 8, lines 6-8, page 9, lines 20-26 and page 10, lines 15-20 and lines 24-25. New claims 31-37, in addition to pending claims 1-9 and 25-30 recite a novel and nonobvious biomolecule capture device that is neither anticipated nor obvious over the teachings, alone or in combination, of the Singh et al., Johnson and Kinsella et al. references. Consideration of new claims 30-37, reconsideration of claims 1-9 and 25-29 and allowance of the pending claims are requested.

Conclusion

Applicants have submitted additional new claims 31-37. Entry and consideration of the new claims and reconsideration and allowance of all pending claims in light of the amendments previously submitted and the information concerning the differences between the cited references and the claims of the Subject Application discussed during the telephone interview of May 23, 2006 and summarized herein, are earnestly solicited. If the undersigned can be of assistance in advancing the Subject Application to allowance, the Examiner may contact the undersigned at the number set forth below.

Respectfully submitted,



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